Journal of the American College of Cardiology Vol. 58, No. 14, 2011

Published by Elsevier Inc.
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.05.048

EDITORIAL COMMENT

Coronary Angiographic Evaluation of Low-Risk Chest Pain in the Emergency Department

CT-STAT, or Maybe Not Quite That Fast?*

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Coronary computed tomographic angiography (CCTA) is evolving into a mature imaging modality for assessment of patients with acute chest pain in the emergency department (ED). More than 1,000 patients have been studied in the ED setting in both single-center and multicenter trials, not including the results of the CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial published by Goldstein et al. (1) in this issue of the *Journal*. The results

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of these prior studies demonstrate a pooled sensitivity of 92%, specificity of 89%, and a very high negative predictive value (NPV) of 99% (2). The positive predictive values for detecting significant coronary artery disease (CAD) have been moderate, ranging from 33% to 95% with a pooled estimate of 48%. Furthermore, the concordance between obstructive CAD by CCTA, and ischemia by myocardial perfusion imaging (MPI) has been low, ranging from 29% to 44% (3). However, because of its excellent NPV, CCTA has been particularly useful to exclude significant stenoses in patients presenting to the ED with chest pain and low-intermediate likelihood of CAD. Several studies have demonstrated very low event rates at 1 year of follow-up in patients either without CAD or with minimal nonobstructive plaque (4). As CCTA can be performed rapidly, it has the potential to significantly impact the triage of chest pain patients in the ED. Myocardial perfusion imaging has been the predominant noninvasive approach to detecting CAD among chest pain patients (5).

The findings of the multicenter CT-STAT trial (1) confirm the single-center study by Goldstein et al. (6). In the multicenter trial, 361 patients with acute chest pain in the ED were randomly assigned to CCTA and 338 to single-positron emission computed tomography (SPECT) MPI. The CCTA strategy resulted in a 54% reduction in time to diagnosis compared with MPI (2.9 h vs. 6.3 h), and costs of care were 38% lower for the CCTA group. The 2 strategies showed no difference in freedom from major adverse cardiac events at 6 months of follow-up.

It is notable that the CT-STAT study utilized a rest-stress MPI protocol that may have contributed to both the longer time to diagnosis and the cost for the stress imaging strategy. While this was the typical protocol for MPI in the centers included in the trial at the time, in recent years, EDs and chest pain centers are increasingly utilizing stress-only protocols for low-risk patients without acute electrocardiography (ECG) changes. Stress-only MPI protocols have been evaluated in several studies with large patient populations, and no significant differences in mortality have been found for patients with a normal stress-only study as compared with patients who had normal rest-stress study (7). Thus, an additional rest MPI is not necessary in patients who have a normal initial gated-stress MPI study. Had such a protocol been used in the CT-STAT study, the time to diagnosis would have been substantially shortened, as 89.9% of the patients in the SPECT arm had normal MPI studies.

Several technical advances are improving the ability of SPECT MPI to diagnose ischemia faster and include ultrafast cameras that employ innovative gantry designs, cadmium zinc telluride solid-state detectors, and novel iterative reconstruction algorithms that enable rest and stress imaging to each be performed in <5 min (8,9). Use of such ultrafast SPECT cameras would further decrease the time to diagnosis of CAD for patients being evaluated for chest pain in the ED.

Alternatively, an exercise ECG stress test alone without concomitant cardiac imaging would be feasible for patients at very low risk for an acute coronary syndrome (ACS) and who likely have very good functional capacity. We found that in patients who achieved a high workload (i.e., ≥10 metabolic equivalents) without ST-segment depression, the prevalence of significant ischemia comprising 10% or more of the left ventricle by MPI was 0%, with only 1 cardiac death during 2.6 years of follow-up (10,11). This strategy would likely be more cost-effective than any imaging strategy.

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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Another advantage of CCTA reported by Goldstein et al. (1) was a reduced radiation dose compared with SPECT. The radiation doses of both CCTA and SPECT MPI studies have dropped significantly with equipment and protocol advancements. Several radiation dose-sparing strategies for CCTA, including tube current modulation, reduced tube voltage for nonobese patients, and prospective gating techniques, have been widely employed in clinical practice. However, it is important to note that these strategies have limitations in subjects who have elevated body mass index (>35 kg/m^2), elevated heart rate (>70 beats/min), or irregular heart rates. New technologies such as 320-row detector computed tomography can perform a CCTA in a single heart beat at a dose of approximately 4 to 5 mSv (12). Recently, high-pitch coronary protocols using a dual-source CCTA scanner have demonstrated doses of <1 to 2 mSv (13). The radiation dose with radionuclide MPI has also been dropping, and newer ultrafast cameras have doses as low as 4.2 mSv for a stress-only protocol (8). Even with older equipment, a stress-only protocol would significantly reduce radiation dose. Thus, using the most up-to-date CCTA protocols, and employing stress-only MPI protocols, both arms of this study would expose patients to a significantly lower radiation dosage.

The ongoing PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial, which is the largest National Institutes of Health–sponsored multicenter comparative effectiveness imaging trial with a targeted enrollment of 10,000, will provide further insight into the diagnostic accuracy and cost-effectiveness of a diagnostic strategy using an anatomic assessment with CCTA versus a functional assessment with conventional stress testing. Although this study is not in the ED setting, it will provide important additional information about the relative merits of using an anatomical versus functional assessment for diagnosing CAD.

A few areas of active research may further improve the diagnostic utility of CCTA. Stress perfusion imaging using CCTA has shown promise, but to date these protocols have significant radiation burden (14). Plaque characterization may improve the diagnostic utility of CCTA; however, these techniques are still in the development and clinical validation stage (15). Molecular imaging with positron-emission tomography (PET)–computed tomography may also hold potential for identifying inflammation and detecting vulnerable plaques (16), and could provide a comprehensive assessment of both coronary anatomy, and myocardial perfusion (17).

Other imaging techniques hold promise for the detection of CAD and ACS in patients presenting to the ED with chest pain. Cardiac magnetic resonance (CMR) has been shown to accurately identify patients with possible ACS with a sensitivity and specificity for detecting ACS of using resting perfusion, ventricular function, and gadolinium enhancement of 84% and 85%, respectively (18). The addition of edema imaging increased the specificity, positive predictive value, and overall accuracy to 96%, 85%, and 93%, respectively (19). Furthermore, patients with a normal adenosine stress study had no subsequent diagnosis of CAD or major adverse cardiac events at 1 year (20). A recent comparison of 32-channel 3-T coronary magnetic resonance angiography versus 64-slice CCTA demonstrated similar diagnostic accuracy for detecting obstructive CAD, and both techniques identified all cases of left main and 3-vessel disease (21). Thus, CMR can provide a comprehensive assessment of function and coronary anatomy. Minimal data are available for assessing PET MPI in the ED setting; however, PET is associated with lower radiation doses (from 2 mSv for $^{13}NH_3$ to 3.7 mSv for a ^{82}Rb MPI [22]), improved data acquisition efficiency (rest-stress Rb-82 PET MPI study can be performed in <15 min), and improved diagnostic accuracy and certainty as compared with SPECT MPI (23). Although PET is more costly than SPECT, the overall cost of this diagnostic strategy is unclear, as it may reduce additional testing from the improved test characteristics.

In summary, the CT-STAT trial provides additional evidence for the excellent NPV of CCTA in patients at low risk for an ACS or at low-intermediate risk of having CAD as the cause of the chest pain syndrome, and who are eligible for this imaging approach. A substantial number of patients presenting with chest pain in the ED, as described by Goldstein et al. (1), are not eligible for CCTA or would benefit more from a functional imaging approach. Advances in both CCTA and MPI are improving the diagnostic accuracy of these imaging technologies, with concomitant reduction in radiation exposure. Both the anatomic diagnostic strategy and the physiologic stress imaging strategy yield similar outcomes with respect to predicting cardiac events. The true differences in time to diagnosis and costs between these 2 approaches will be determined in future studies that employ such state-of-the-art technology and with enhanced interpretive experience of physicians reading these studies. Other technologies such as CMR and contrast echocardiography may also play a future role in this patient population. Finally, it should be emphasized that the most cost-effective strategy is exercise ECG testing alone as the first test, with no imaging performed for patients with atypical chest pain, patients with a normal resting ECG, and patients who attain high exercise heart rates and workloads without associated ischemic ST-segment depression.

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REFERENCES

1. Goldstein JA, Chinnaiyan KM, Abidov A, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol 2011;58:1414–22.

2. Cury RC, Feuchtner G, Mascioli C, et al. Cardiac CT in the emergency department: Convincing evidence, but cautious implementation. J Nucl Cardiol 2011;18:331–41.
3. Hachamovitch R, Di Carli MF. Nuclear cardiology will remain the "gatekeeper" over CT angiography. J Nucl Cardiol 2007;14:634–44.
4. Hulten EA, Carbonaro S, Petrillo SP, Mitchell JD, Villines TC. Prognostic value of cardiac computed tomography angiography a systematic review and meta-analysis. J Am Coll Cardiol 2011;57:1237–47.
5. Hendel R, Dahdah N. The potential role for the use of cardiac computed tomography angiography for the acute chest pain patient in the emergency department: a cautionary viewpoint. J Nucl Cardiol 2011;18:163–7.
6. Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863–71.
7. Chang SM, Nabi F, Xu J, Raza U, Mahmarian JJ. Normal stress-only versus standard stress/rest myocardial perfusion imaging: similar patient mortality with reduced radiation exposure. J Am Coll Cardiol 2011;55:221–30.
8. Duvall WL, Croft LB, Godiwala T, Ginsberg E, George T, Henzlova MJ. Reduced isotope dose with rapid SPECT MPI imaging: initial experience with a CZT SPECT camera. J Nucl Cardiol 2010;17:1009–14.
9. Garcia EV, Faber TL, Esteves FP. Cardiac dedicated ultrafast SPECT cameras: new designs and clinical implications. J Nucl Med 2011;52:210–7.
10. Bourque JM, Charlton GT, Holland BH, Belyea CM, Watson DD, Beller GA. Prognosis in patients achieving ≥10 METS on exercise stress testing: was SPECT imaging useful? J Nucl Cardiol 2011;18:230–7.
11. Bourque JM, Holland BH, Watson DD, Beller GA. Achieving an exercise workload of > or = 10 metabolic equivalents predicts a very low risk of inducible ischemia: does myocardial perfusion imaging have a role? J Am Coll Cardiol 2009;54:538–45.
12. Einstein AJ, Elliston CD, Arai AE, et al. Radiation dose from single-heartbeat coronary CT angiography performed with a 320-detector row volume scanner. Radiology 2011;254:698–706.
13. Leschka S, Stolzmann P, Desbiolles L, et al. Diagnostic accuracy of high-pitch dual-source CT for the assessment of coronary stenoses: first experience. Eur Radiol 2009;19:2896–903.
14. Blankstein R, Shturman LD, Rogers IS, et al. Adenosine-induced stress myocardial perfusion imaging using dual-source cardiac computed tomography. J Am Coll Cardiol 2009;54:1072–84.
15. Madder RD, Chinnaiyan KM, Marandici AM, Goldstein JA. Features of disrupted plaques by coronary computed tomographic angiography: correlates with invasively proven complex lesions. Circ Cardiovasc Imaging 2011;4:105–13.
16. Rogers IS, Nasir K, Figueroa AL, et al. Feasibility of FDG imaging of the coronary arteries: comparison between acute coronary syndrome and stable angina. J Am Coll Cardiol Img 2011;3:388–97.
17. Di Carli MF, Dorbala S, Curillova Z, et al. Relationship between CT coronary angiography and stress perfusion imaging in patients with suspected ischemic heart disease assessed by integrated PET-CT imaging. J Nucl Cardiol 2007;14:799–809.
18. Kwong RY, Schussheim AE, Rekhraj S, et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. Circulation 2003;107:531–7.
19. Cury RC, Shash K, Nagurney JT, et al. Cardiac magnetic resonance with T2-weighted imaging improves detection of patients with acute coronary syndrome in the emergency department. Circulation 2008;118:837–44.
20. Ingkanisorn WP, Kwong RY, Bohme NS, et al. Prognosis of negative adenosine stress magnetic resonance in patients presenting to an emergency department with chest pain. J Am Coll Cardiol 2006;47:1427–32.
21. Hamdan A, Asbach P, Wellnhofer E, et al. A prospective study for comparison of MR and CT imaging for detection of coronary artery stenosis. J Am Coll Cardiol Img 2011;4:50–61.
22. Senthamizhchelvan S, Bravo PE, Esaias C, et al. Human biodistribution and radiation dosimetry of 82Rb. J Nucl Med 2010;51:1592–9.
23. Di Carli MF, Dorbala S, Meserve J, El Fakhri G, Sitek A, Moore SC. Clinical myocardial perfusion PET/CT. J Nucl Med 2007;48:783–93.

Key Words: acute chest pain ■ coronary computed tomography ■ cost of care ■ diagnostic effectiveness ■ emergency department.